Non-Technical Abstract

In this study approximately 18 patients will be treated with an investigational vaccine for melanoma called Synchrotope MA2M to find out if it is safe and what side effects occur when the vaccine is injected into a lymph gland in the groin using a needle and a small pump. The Synchrotope MA2M is made from DNA, a natural substance from which the genes in all of our cells are made. The vaccine DNA includes the body's genetic blueprint for Melan-A/MART-l, a substance present in most melanomas, which can be recognized by the immune system. It is hoped that administration of this DNA vaccine will cause shrinkage of melanoma or delay the growth of melanoma by boosting immunity to Melan-A/MART-l on melanoma cells, although this cannot be determined in advance, since there is little experience with similar vaccines in other melanoma patients.

In this trial, patients' blood cells will be tested for the expression of HLA-A2 blood type, which must be positive for patients to be eligible for this study. A preserved piece of patients' tumors will be tested for the presence of Melan-A/MART-l, the substance being vaccinated against. The presence of Melan-A/MART-l on the tumor is required for entry to this trial. Patients will undergo a series of tests including CT scans and an MRI scan to determine the size and extent of their tumor. To be eligible for this trial, patients must also have adequate function of the major organs and not have any serious infections.

Eligible patients will have an ultrasound test, which consists of painlessly bouncing sound waves off the body to locate a lymph gland the size of a dime in the groin. The lymph gland will then be punctured with a needle into which a thin plastic tube or catheter will be placed, and the needle removed. The plastic catheter will then be taped to the skin, and a small pump the size of a deck of cards will be used to pump the DNA vaccine continuously into the lymph gland for 96 hours. The correct position of the tip will be checked by another ultrasound at the end of the fourth day of each cycle of treatment. Patients on this trial will receive increasing doses of the DNA vaccine in groups of six patients at each dose.

After the four-day or 96 hour period of injection of the DNA vaccine, there will be a nine-day rest period for a total of two weeks in a cycle of treatment. The treatment cycle will be repeated four times over eight weeks. Follow-up visits to the physician will be required after eight weeks from starting treatment. The total time of the study is at least eight weeks.

No life threatening side effects or deaths were seen with previous tests of vaccines injected into the lymph nodes in patients with metastatic melanoma, including a DNA plasmid. The side effects related to injection of other melanoma DNA vaccines under the skin and in the veins included headache, fevers, weakness, joint pains and a rash that resolved without therapy. In animal testing, the melanoma DNA vaccine had few significant toxic side effects. It is possible, but very unlikely, that vaccination with a DNA vaccine may induce inflammation in the retina of the eye and even cause blindness. Melan-A/MART-1 is also present on normal human skin pigment cells. It is possible, but very unlikely, that vaccination with a DNA vaccine may induce areas of loss of the skin pigment called vitiligo. Swelling of the joint with inflammation, pain, rashes and abnormalities of kidney and liver function might occur.

It is possible that there might be damage to the lymph gland that is injected. The lymph glands might become swollen or tender, or bleeding may occur. This has shown to be temporary, with the lymph glands returning to normal after the injections. The plastic catheter will be inserted in a sterile manner into the lymph gland, but infection at the injection site might occur.

After eight weeks of treatment, patients will have repeated x-rays and scans to measure their tumors. Blood samples (one tablespoon each) to measure important organ functions will be performed every other week beginning on the first day of treatment. Special blood tests (seven tablespoons each) to measure the level of function of the immune system will be performed before treatment begins, just after the second treatment cycle, and just after the fourth treatment cycle. If there is evidence that the tumor has stayed the same or shrunk in response to the therapy, a repeated cycle of treatment with the DNA vaccine may be given.